

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 1 of 13

Complete if Known

Application Number	10/575,132
Filing Date	July 7, 2006
First Named Inventor	Sarah Donald
Art Unit	1612
Examiner Name	Chris E. Simmons
Attorney Docket Number	13566.105014

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
		US-20020137663	9/26/2002	Forman et al.	
		US-20040019027	1/29/2004	Forman et al.	
		US- 20040002602	01/01/04	Francesch et al.	
		US- 20060030571	2/9/2006	Rinehart	
		US- 20060094687	5/4/2006	Beijnen	
		US- 20070004691	1/4/2007	Donald	
		US- 20070082856	4/12/2007	Gianni	
		US- 20070128201	6/7/2007	D'Incalci et al.	
		US- 5,089,273	2/18/1992	Rinehart et al.	
		US- 5,149,804	9/22/1992	Rinehart et al.	
		US-5,256,663	10/26/1993	Rinehart et al.	
		US- 5,478,932	12/26/1995	Rinehart et al.	
		US- 5,552,544	9/3/1996	Brana Fernandez et al.	
		US- 5,654,426	8/5/1997	Rinehart et al.	
		US- 5,721,362	2/24/1998	Corey et al.	
		US- 5,985,876	11/16/1999	Rinehart et al.	
		US- 6,124,293	9/26/2000	Rinehart et al.	
		US- 6,153,590	11/28/2000	Andersen et al.	
		US- 7,241,892	07/10/07	Cuevas et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
		WO 99/58125	11/18/1999	Rinehart et al.		
		WO 99/51238	10/14/1999	Rinehart et al.		
		WO 00/69862	11/23/2000	Cuevas et al.		
		WO 01/77115	10/18/2001	Flores et al.		
		WO 01/87894	11/22/2001	Cuevas et al.		
		WO 02/064843	8/22/2002	Haygood et al.		
		WO 02/36135	05/10/2002	Takahashi et al.		
		WO 03/039571	5/15/2003	Jimeno et al.		
		WO 05/49029	06/02/2005	Gianni et al.		
		WO 05/49030	6/2/2005	Rowinsky et al.		
		WO 05/49031	6/2/2005	Rybak et al.		
		WO 06/35244	4/6/2006	Allavena et al.		
		WO 06/46080	5/4/2006	Gilles et al.		

Examiner
Signature

/Chris Simmons/

Date
Considered

08/13/2008

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				Examiner Name	Chris E. Simmons
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NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/C.S./		Akers, "Excipient -Drug Interactions in Parenteral Formulations," Journal of Pharmaceutical Sciences, 91(11), pp. 2283-2300, Nov. 2002	
/C.S./		Barrera, H. et al., "Interaction of ET-743 and standard cytotoxic agents against a panel of human tumor cell lines," Proceedings of the American Association for Cancer Research, Volume 40, page 591, Abstract No. 3896, March 1999	
/C.S./		Biroccio et al., "Telomere Dysfunction Increases Cisplatin and Ecteinascidin-743 Sensitivity of Melanoma Cells," Molecular Pharmacology, 63:632-638 (2003)	
/C.S./		Blay et al., "Combination of Trabectedin and Doxorubicin for the Treatment of Patients with Soft Tissue Sarcoma: Safety and Efficacy Analysis," 43rd annual ASCO meeting, June 1-5, 2007	
/C.S./		Bonfanti et al., "Effect of Ecteinascidin-743 on the Interaction Between DNA Binding Proteins and DNA." Anticancer Drug Des. 14, 179-86, 1999	
/C.S./		Bowman, A. et al., "Phase I clinical and pharmacokinetic (PK) study of ecteinascidin-743 (ET-743) given as a one hour infusion every 21 days," Annals Oncology, Abstract 452, 1998	
/C.S./		Brandon et al., "In-vitro Cytotoxicity of ET-743 (Trabectedin, Yondelis), a Marine Anti-cancer Drug, in the Hep G2 Cell Line: Influence of Cytochrome P450 and Phase II Inhibition, and Cytochrome P450 Induction, Anti-cancer Drugs, 16:935-943 (2005)	
/C.S./		Burstein et al., "Phase I study of Doxil and Vinorelbine in Metastatic Breast Cancer," Annals of Oncology, vol. 10, pages 1113-1116, 1999, XP8086751	
/C.S./		European Agency for the Evaluation of Medicinal Products, "Committee for Proprietary Medicinal Products Summary of Opinion for Yondelis", November 20, 2003	
/C.S./		Corey et al., "Enantioselective Total Synthesis of Ecteinascidin 743", J. Am. Chem. Soc., 118, 9202-9203, 1996	
/C.S./		Cvitkovic, E. et al., "Final results of a phase I study of ecteinascidin-743 (ET-743) 24 hour (h) continuous infusion (CI) in advanced solid tumors (AST) patients (pts)," 1999 ASCO Annual Meeting Proceedings, Abstract No. 690, May 15-18, 1999	
/C.S./		Cvitkovic, E. et al., "Ecteinascidin-743 (ET-743) 24 hour continuous intravenous infusion (CI) phase I study in solid tumors (ST) patients," Annals Oncology, Abstract 456, 1998	
/C.S./		Delaloge et al., "Ecteinascidin (ET-743) in heavily pretreated refractory sarcomas: Preliminary evidence of activity," Eur. J. Cancer, vol. 35, suppl. 4, page S271, Abstract No. 1080, Sept 15, 1999	

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/C.S./		Delaloge, S. et al., "Ecteinascidin-743: A Marine-Derived Compound in Advanced Pretreated Sarcoma Patients-Preliminary Evidence of Activity", J. of Clinical Oncology, vol. 19, no. 5, pp. 1248-1255, 2001	
/C.S./		DeVita et al., "Combination Versus Single Agent Chemotherapy: A Review of the Basis for Selection of Drug Treatment of Cancer", Cancer, vol. 35, pp. 98-110, 1975	
/C.S./		D'Incalci et al., "Mode of action of Ecteinascidin-743 (ET-743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, pages 3872s-3873s, Abstract of Plenary Session 7, November 16-19, 1999	
/C.S./		D'Incalci et al., "The Combination of ET-743 and Cisplatin (DDP): From a Molecular Pharmacology Study to a Phase I Clinical Trial," from the AACR Annual Meeting of April 6-10, 2002, Abstract 404	
/C.S./		D'Incalci et al., "In human tumor xenografts the resistance to ET-743 or to cisplatin can be overcome by giving the two drugs in combination," European Journal of Cancer, 38, Suppl. 7, 34 (November 2002)	
/C.S./		D'Incalci et al., "Preclinical and Clinical Results with the Natural Marine Product ET-743," Expert Opin. Investig. Drugs, 12(11):1843-1853 (2003)	
/C.S./		D'Incalci et al., "The combination of yondelis and cisplatin is synergistic against human tumor xenografts," European Journal of Cancer 39: 1920-1926 (2003)	
/C.S./		Dorr and Van Hoff, "Doxorubicin," Cancer Chemotherapy Handbook, 1994, pp. 395-416	
/C.S./		"Doxil (doxorubicin HCl Liposome Injection) Product Information", October 10, 2004, pages 1-16, XP002389462, <<web.archive.org/web/20041009180>>	
/C.S./		Drugs Fut., "Ecteinascidin-743" vol. 22, no. 11, page 1279, 1997	
/C.S./		Eckhardt et al., "In vitro Studies of a Novel Marine Cytotoxic, Ecteinascidin (ET-743)," New Drugs and Pharmacology, Annals of Oncology, 7 (Suppl. 5), 131, Abstract 632P (1996)	
/C.S./		Endo et al., "Total Synthesis of Ecteinascidin 743", J. Am. Chem. Soc., 124, 6552-6554, 2002	

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		Erba et al., "Synergistic cytotoxic effect of ET-743 and cisplatin," Clinical Cancer Research, Vol. 6, Abstract 209, November 7-10, 2000	
/C.S./		Erba et al., "Combination of yondelis (ET-743) and oxaliplatin in experimental ovarian cancer," from the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics of Nov. 17-21, 2003, Abstract C247	
/C.S./		Erba et al., "ET-743 and Cisplatin (DDP) Show in Vitro and in Vivo Synergy Against Human Sarcoma and Ovarian Carcinoma Cell Lines," from the AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics of October 29 – November 2, 2001, Abstract 406.	
/C.S./		Erlichman, C., "18: Pharmacology of Anticancer Drugs," The Basic Science of Oncology, 2nd edition, Tannock et al., editors, McGraw-Hill, New York, pages 317-337, 1992	
/C.S./		FDA approved label for Pharmacia and Upjohn's Doxorubicin Hydrochloride for Injection (May 8, 2003)	
/C.S./		Faircloth et al., "In Vivo Combinations of Chemotherapeutic Agents with Ecteinascidin 743 (ET743) Against Solid Tumors," from the Proceedings AACR-NCI-EORTC of November 2001, Abstract 387	
/C.S./		Faircloth et al., "Dexamethasone Potentiates the Activity of Ecteinascidin 743 in Preclinical Melanoma and Osteosarcoma Models," Abstract and Presentation 379 (2002)	
/C.S./		Faulkner et al., "Symbiotic Bacteria in Sponges: Sources of Bioactive Substances," Drugs from the Sea, Fusetani, N. (ed.), Basel Karger, 2000, pp. 107-119	
/C.S./		Fayette et al., "ET-743: a Novel Agent with Activity in Soft-Tissue Sarcomas," Current Opinion in Oncology, 18:347-353 (2006)	
/C.S./		Fourouzesh, B. et al., "Phase I and pharmacokinetic study of the marine-derived DNA minor groove binder ET-743 on a weekly x3 every-4-week schedule in patients with advanced solid malignancies," Proceedings of the 2001 AACR-NCI-EORTC International Conference, Abstract No. 209, October 29-November 2, 2001	
/C.S./		Fourouzesh, B. et al., "Phase I and pharmacokinetic study of ET-743, a minor groove DNA binder, administered weekly to patients with advanced cancer," Proc Am Soc Clin Oncol, vol 20, 2001 ASCO Annual Meeting Proceedings, Abstract No. 373, 2001	
/C.S./		Fourouzesh, B., et al., "Phase I and pharmacokinetic study of ET-743, a minor groove DNA binder, administered weekly to patients with advanced cancer," European Journal of Cancer, ECCO 11, volume 37, supplement 6, Abstract No. 106, October 21-25, 2001	
/C.S./		Friereich et al., "Quantitative Comparison of Toxicity of Anticancer Agents in Mouse, Rat, Hamster, Dog, Monkey, and Man," Cancer Chemotherapy Reports, 50:4, May 1966, pp.219-245	

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/C.S./		Fukuyama et al., "Total Synthesis of Saframycin A," J. Am. Chem. Soc., 112, 3712-3713, 1990	
/C.S./		Fukuyama et al., "Stereocontrolled Total Synthesis of Saframycin B," J. Am. Chem. Soc., 104, 4957-4958, 1982	
/C.S./		Garcia-Carbonero et al., "Population pharmacokinetics of ecteinascidin 743 in patients with advanced soft tissue sarcoma," Clinical Cancer Research, vol. 6, Supplement, Abstract 211, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
/C.S./		Garcia Gravalos, M.D., et al., "In vitro schedule-dependent cytotoxicity by ecteinascidin 743 (ET-743) against human tumor cells," 23rd European Society for Medical Oncology Congress, Abstract No. 652, November 6-10, 1998	
/C.S./		Ghielmini, M. et al., "Schedule-dependent myelotoxicity induced in vitro by the new marine derived minor groove interacting agent ecteinascidin 743," ECCO, vol. 9, Abstract No. 807, September 17, 1997	
/C.S./		Ghielmini, M. et al., "In vitro schedule-dependency of myelotoxicity and cytotoxicity of Ecteinascidin 743 (ET-743)," Annals of Oncology, vol. 9, pages 989-993, 1998	
/C.S./		Gianni et al. "Definition of the Least Toxic Sequence and Optimal Therapeutic Dose of Yondelis® in Combination with Doxorubicin in Patients with Untreated Metastatic Soft Tissue Sarcomas and Advanced Pre-Treated Anthracycline," Clinical Cancer Research, Vol. 9, No. 16, pg. 6081S (December 2003)	
/C.S./		Giovanna et al., "Importance of DNA repair mechanisms for the sensitivity of tumor cells to ET-743," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 303, November 16-19, 1999	
/C.S./		Goodman & Gilman's The Pharmaceutical Basis of Therapeutics, page 36, 1975	
/C.S./		Goodman & Gilman's The Pharmaceutical Basis of Therapeutics (9 th edition), page 930, 1996	
/C.S./		Goodman & Gilman's The Pharmaceutical Basis of Therapeutics (9 th edition), pages 1230. 1232, 1996	
/C.S./		Gore et al., "Phase I Combination Study of Trabectedin and Capecitabine in Patients With Advanced Malignancies," Poster Presentation, 42nd ASCO Annual Meeting held on June 2-6, 2006, Atlanta, Georgia	
/C.S./		Grever et al., "The National Cancer Institute: Cancer Drug Discovery and Development Program", Seminars in Oncology, vol. 19, no. 6, 622-638, December 1992	

Crossed out items were not considered because

918288 v1 it is unclear which documents correspond to these items.
ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /C.S./

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/C.S./		Grosso et al., "Steroid Premedication Markedly Reduces Liver and Bone Marrow Toxicity of Trabectedin in Advanced Sarcoma," European Journal of Cancer 42:10, 1484-1490 (2006)	
/C.S./		Gurtler, J.S. et al., "Trabectedin in third line breast cancer: a multicenter, randomized, phase II study comparing two administration regimens," Journal of Clinical Oncology, 2005 ASCO Annual Meeting Proceedings, vol. 23, no. 16S, part I of II (June 1 Supplement), Abstract No. 625, 2005	
/C.S./		Hendriks, H.R. et al., "High antitumor activity of ET743 against human tumor xenografts from melanoma, non-small-cell lung and ovarian cancer," Annals of Oncology, vol. 10, pages 1233-1240, 1999	
/C.S./		Hidalgo, M., et al., "A phase I and pharmacokinetic (PK) study of ET-743, a novel marine groove binder of marine origin administered on a daily x 5 schedule," 23rd European Society for Medical Oncology Congress, Abstract No. 613P, November 6-10, 1998	
/C.S./		Hillebrand, M.J.X. et al., "Pharmacokinetics of ecteinascidin-743 (ET-743) in three phase I studies," Annals Oncology, Abstract No. 455, 1998	
/C.S./		Holmes, "Paclitaxel Combination Therapy in the treatment of Metast Breast Cancer: A Review," Seminars in Oncology, vol. 23, pp. 46-56, 1996	
/C.S./		Hornicek et al., "In vitro effect of the tetrahydroisoquinoline alkaloid Ecteinascidin-743 (ET-743) on chondrosarcoma (CHSA) cells," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 304, November 16-19, 1999	
/C.S./		Hornicek et al., "Effect of Ecteinascidin-743 and Plasminogen related Protein B on a Human Chondrosarcoma Xenograft Tumor in Mice," Clinical Cancer Research, Vol. 7 Supplement P3734S-3734S, Abstract 398 (November 2001)	
/C.S./		Ishikawa et al., "Tumor Selective Delivery of 5-Fluorouracil by Capecitabine," Biochemical Pharmacology, vol. 55, pp. 1091-1097, 1998	
/C.S./		Izbicka, E. et al., "In vitro antitumor activity of the novel marine agent, Ecteinascidin-743 (ET-743, NSC- 648766) against human tumors explanted from patients," Annals of Oncology, vol. 9, pages 981-987, 1998	
/C.S./		Jimeno, J.M. et al., "Enhancing the preclinical in vivo antitumor activity of ecteinascidin 743, a marine natural product currently in phase II clinical trials," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, Volume 5, page 3790S, Abstract No. 306, November 16-19, 1999	
/C.S./		Jimeno et al., "Pharmacokinetics (PK)/Pharmacodynamic (PD) Relationships in Patients (PT) Treated With Ecteinascidin-743 (ET-743) Given As 24 Hours Continuous Infusion (CI)," Journal of Clinical Oncology, ASCO Annual Meeting Proceedings, Abstract No. 744, May 15-18, 1999	

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/C.S./		Jimeno, J. et al., "Phase I and pharmacokinetic (PK) study of Et-743, a novel minor groove binder of marine origin on a daily [times] 5 schedule," 1998 ASCO Annual Meeting Proceedings, Abstract No. 737, 1998	
/C.S./		Jimeno, Jose et al., "Adding Pharmacogenomics to the Development of New Marine-Derived Anticancer Agents," Journal of Translational Medicine, volume 4, issue 3, January 9, 2006, downloaded from the internet website: << http://www.translational-medicine.com/content/4/1/3 >>	
/C.S./		Jin et al., "The antitumor agent Ecteinascidin 743 (ET743), inhibits transcriptional activation of the MDR1 Gene by multiple inducers," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 302, November 16-19, 1999	
/C.S./		Jin et al., Ecteinascidin-743, A Transcription-Targeted Chemotherapeutic that Inhibits MDR I Activation. Proc. Natl. Acad. Sci. USA, 97, 6775-9, 2000	
/C.S./		Kanzaki et al., "Microsatellite Instability (MSI) Induced by Ecteinascidin743 and Protection with Aspirin," from the 93rd Annual Meeting of the American Association for Cancer Research, Abstract 5382 (April 6-10, 2002), Vol. 43, March 2002, page 1087	
/C.S./		Kovalcik et al., "The Stability of Cyclophosphamide in Lyophilized Cakes. part I. Mannitol, Lactose, and Sodium Bicarbonate as Excipients," Journal of Parenteral Science and Technology, vol. 42, no. 1, Jan-Feb. 1988, pp. 29-37	
/C.S./		Laverdiere et al., "Phase II Study of Ecteinascidin 743 In Heavily Pretreated Patients with Recurrent Osteosarcoma", Cancer, American Cancer Society, Philadelphia, PA, August 15, 2003, vol. 98:4, pages 832-840, XP002314512	
/C.S./		Leonetti et al., "Antitumoral Effect of the G-quadruplex Interactive Compound RHPS4 on Human Melanoma Cells Possessing Relatively Long Telomeres," from the Proceedings of the AACR, Volume 45, March 2004	
/C.S./		Lopez-Lazaro et al., "Exploratory evaluation of the potential predictors for dose-limiting toxicities (DLTs) in patients treated with Ecteinascidin-743 (ET-743) as a 24-h intravenous (iv) infusion every 3 weeks and its relationship to pharmacokinetics (PK)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 308, November 16-19, 1999	
/C.S./		Lyass et al., "Phase I Study of Doxil-Cisplatin Combination Chemotherapy in Patients with Advanced Malignancies," Clinical Cancer Research, vol. 7, pages 3040-3046, October 2001, XP8086753	

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/C.S./		Maier et al., "In vitro inhibition of endothelial cell growth by the antiangiogenic drug AGM-1470 (TNP-470) and the antiendoglin antibody TEC-11," Anti-Cancer Drugs, vol. 8, pp. 238-244, 1997		
/C.S./		Magro et al., "The Role of PARP and PARP Inhibitors in Yondelis (Trabectedin) Mediated Cytotoxicity," Abstract and Presentation from the AACR Annual Meeting, April 17, 2007		
/C.S./		Manzanares et al., "Advances in the Chemistry and Pharmacology of Ecteinascidins, A Promising New Class of Anticancer Agents," Curr. Med. Chem. - Anti-Cancer Agents, 2001, vol. 1, pp. 257-276		
/C.S./		Martinez et al., "Phthalascidin, A Synthetic Antitumor Agent with Potency and Mode of Action Comparable to Ecteinascidin 743." Proc. Natl. Acad. Sci. USA 96; 3496-501, 1999		
/C.S./		Martinez, E. J. et al., "A New, More Efficient, and Effective Process for the Synthesis of a Key Pentacyclic Intermediate for Production of Ecteinascidin and Phthalascidin Antitumor Agents." Org. Lett. 2, 993-6, 2000		
/C.S./		McLeod, "Clinically relevant drug-drug interactions in oncology," Br. J. Clin. Pharmacol., 45:539-544 (1998).		
/C.S./		McMeekin, D.S. et al., "Final results of a phase II study of weekly trabectedin in second/third line ovarian carcinoma," Journal of Clinical Oncology, 2005 ASCO Annual Meeting Proceedings, Vol. 23, No. 16S, Part I of II (June 1 Supplement), Abstract No. 5011, May 13-17, 2005		
/C.S./		Meco et al., "Effective combination of ET-743 and doxorubicin in sarcoma: preclinical studies," Cancer Chemother. Pharmacol. 52: 131-138 (2003).		
/C.S./		Meco et al., "The combination of ET-743 and Irinotecan is active in preclinical models in rhabdomyosarcoma," presented at the 16th EORTC-NCI-AARC Symposium on Molecular Targets and Cancer Therapeutics held in Geneva on September 28 - October 1, 2004.		
/C.S./		Menchaca et al., "Synthesis of Natural Ecteinascidins (ET-729, ET-745, ET-759B, ET-736, ET-637, ET-594) from Cyanosafraicin B," J. Org. Chem., published on web October 21, 2003, pp. 8859-8866		
/C.S./		Merck Manual on-line edition version, "Types: Overview of Cancer," 4 pages, downloaded from internet website << http://www.merck.com/mmhe >>, February 2003		
/C.S./		Michaelson, M.D. et al., "Phase II study of three hour, weekly infusion of trabectedin (ET-743) in men with metastatic, androgen-independent prostate carcinoma (AIPC)," Journal of Clinical Oncology, 2005 ASCO Annual Meeting Proceedings, Vol. 23, No. 16S, Part I of II (June 1 Supplement), Abstract No. 4517, May 13-17, 2005		

Substitute for form 1449A/PTO				Complete if Known	
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Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/C.S./		Minuzzo, M. et al., "Interference of Transcriptional Activation by the Antineoplastic Drug Ecteinascidin.743." Proc. Natl. Acad. Sci. USA 97, 6780-4, 2000	
/C.S./		Moore et al., "Sequencing evaluation of ET-743 combinations with standard chemotherapy agents against a panel of human tumor cell lines," Clinical Cancer Research, Vol. 6, Abstract 504 (November 2000)	
/C.S./		Morioka et al., "Antiangiogenesis Treatment Combined with Chemotherapy Produces Chondrosarcoma Necrosis," Clinical Cancer Research, Vol. 9, 1211-1217, March 2003	
/C.S./		Pharma Mar Press Release, "PharmaMar Differs with CPMP Opinion", Pharma Mar Grupo Zeltia, << http://www.pharmamar.com/en/press/news_release.cfm >>, July 24, 2003	
/C.S./		Pharma Mar Press Release, "PharmaMar Receives EMEA Appeal Decision on Yondelis in Soft Tissue Sarcoma", Pharma Mar Grupo Zeltia, << http://www.pharmamar.com/en/press/news_release.cfm >>, November 20, 2003	
/C.S./		Pharma Mar Press Release, "YONDELIS(r) STS-201 Efficacy and Safety Data Presented at ASCO 2007" Pharma Mar Grupo Zeltia, << http://www.pharmamar.com/en/press >>, June 5, 2007	
/C.S./		Pharma Mar Press Release, "The European Commission Authorizes YONDELIS(r) Commercialization for Soft Tissue Sarcoma" Pharma Mar Grupo Zeltia, << http://www.pharmamar.com/en/press >>, September 20, 2007	
/C.S./		Pommier et al., "DNA Sequence- And Structure-Selective Alkylation of Guanine N2 in the DNA Minor Groove by Ecteinascidin 743, a Potent Antitumor Compound from the Caribbean Tunicate Ecteinascidia Turbinata." Biochemistry 35, 13303-9, 1996	
/C.S./		Rinehart, K.L., "Antitumor Compounds from Tunicates." Med. Res. Rev. 20, 1-27, 2000	
/C.S./		Riccardi et al., "Preclinical Activity and Biodistribution of Ecteinascidin 743 (ET-743) and Doxorubicin (DOX) Combinations in Human Rhabdomyosarcoma," from the AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics of October 29 – November 2, 2001, Abstract 405	
/C.S./		Riccardi et al., "Effective Combinations of ET-743 and Doxorubicin for Tumor Growth Inhibitions Against Murine and Human Sarcomas in Athymic Mice," from the Proceedings of the AACR, Vol. 42, Abstract 1132 (March 2001)	
/C.S./		Riccardi et al., "Combination of trabectedin and irinotecan is highly effective in a human rhabdomyosarcoma xenograft," Anti-Cancer Drugs, 16:811-815 (2005).	

Substitute for form 1449A/PTO				Complete if Known	
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/C.S./		Riofrio, M. et al., "Ecteinascidin-743 (ET-743) 24 hours continuous infusion (CI): Clinical and pharmacokinetic phase I study progressive report," 23rd European Society for Medical Oncology Congress, Abstract 639P, November 6-10, 1998	
/C.S./		Robert et al., "Pharmacokinetics of Doxorubicin in Sarcoma Patients," Eur. J. Clin. Pharmacol., vol. 31, pp. 695-699, 1987	
/C.S./		Rosing et al., "Pharmacokinetics (PK) of Ecteinascidin-743 (ET-743) in three different phase I trials," Proceedings of the American Association for Cancer Research, vol. 40, pp 81, abstract no. 542, March 1999	
/C.S./		Ryan, D.P. "Studies with Ecteinascidin-743 (ET-743) A Marine Alkaloid," Cancer Invest, vol. 18 (suppl 1), pp 112, abstract no. 87, January 2000, from the Chemotherapy Foundation Symposium XVII Innovative Cancer Therapy for Tomorrow, November 3-6, 1999, New York, NY	
/C.S./		Ryan, DP et al., "Phase I and Pharmacokinetic Study of Ecteinascidin-743 Administered as a 72 hours Continuous Intravenous Infusion in Patients with Solid Malignancies", Clinical Cancer Research, Vol. 7, pp. 231-242, 2001	
/C.S./		Saito et al., "Synthesis of Saframycins- 3," J. Org. Chem., 54, 5391, 1989	
/C.S./		Sakai et al., "Additional Antitumor Ecteinascidins from a Caribbean Tunicate: Crystal Structures and Activities in vivo," Proc. Natl. Acad. Sci., vol. 89, Dec. 1992, pp. 11456-11460	
/C.S./		Sato et al., "Multicenter Phase II Trial of Weekly Paclitaxel for Advanced or Metastatic Breast Cancer: the Saitama Breast Cancer Clinical Study Group (SBCCSG-01)," Japanese Journal of Clinical Oncology, Vo. 33, no. 8, pp. 371-376, August 2003	
/C.S./		Scotlandi et al., "Effectiveness of Ecteinascidin-743 against Drug-sensitive and -resistant Bone Tumor Cells," Clinical Cancer Research, 8:3893-3903 (December 2002)	
/C.S./		Scotto et al., "Ecteinascidin 743, a novel chemotherapeutic agent that targets transcriptional activation of a subset of genes, including MDR1," Clinical Cancer Research, vol. 6, Supplement, Abstract 210, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
/C.S./		Sessa et al., "Trabectedin for Women with Ovarian Carcinoma After Treatment with Platinum and Taxane Fails," Journal of Clinical Oncology, vol. 23, no. 9, pp. 1867-1874, March 20, 2005	

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/C.S./		Smyth, "Rationale for Drug Combinations," European Journal of Cancer, 39, 1816-1817 (2003)		
/C.S./		Taamma, A. et al., "Ecteinascidin-743 (ET-743) 24 hours continuous infusion (CI): clinical and pharmacokinetic phase I study in solid tumor patients (PTS). Preliminary Results" 1998 ASCO Annual Meeting Proceedings, Abstract No. 890, 1998		
/C.S./		Taamma et al., "Ecteinascidin-743 (ET-743) 24 hour continuous intravenous infusion (CI) phase I study in solid tumors (ST) patients (pts)." Proceedings of the American Association for Cancer Research, vol. 39, pp 323, abstract no. 2207, March 1998		
/C.S./		Taamma, A. et al., "Phase I clinical study of ecteinascidin-743 (ET-743) as a 24 hours continuous intravenous infusion (CI) in patients (pts) with solid tumors (st): A progress report," ECCO, vol. 9, Abstract No. 1119, September 18, 1997		
/C.S./		Taamma et al., "Phase I Clinical Study of ecteinascidin-743 (ET-743) as a 24 hours continuous intravenous infusion (CI) in patients (pts) with solid tumors (st): A progress report," Eur. J. Cancer, 33 Suppl. 8, S247-S248, Abstract, 1997		
/C.S./		Taamma et al., "Ecteinascidin-743 (ET-743) in heavily pretreated refractory sarcomas: early results of the French experience," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 309, November 16-19, 1999		
/C.S./		Taamma et al., "Phase I and Pharmacokinetic Study of Ecteinascidin-743, a New Marine Compound, Administered as a 24 hours Continuous Infusion in Patients with Solid Tumors", J. of Clinical Oncology, vol. 19, no. 5, pp. 1256-1265, March 1, 2001		
/C.S./		Takebayashi et al., "Poisoning of Human DNA Topoisomerase I by Ecteinascidin 743, An Anticancer Drug That Selectively Alkylates DNA in the Minor Groove." Proc. Natl. Acad. Sci. USA 96, 7196-201 1999		
/C.S./		Takebayashi et al., "Multidrug Resistance Induced by DNA Minor Groove Alkylation of Ecteinascidin 743 (Et743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3851s, Abstract 602, November 16-19, 1999		
/C.S./		Takebayashi et al., "Nucleotide excision repair-dependent cytotoxicity of Ecteinascidin 743," Clinical Cancer Research, vol. 6, Supplement, Abstract 207, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000		
/C.S./		Takahashi et al., "Ecteinascidin 743 (ET-743) and doxorubicin produce synergistic cytotoxic effects in soft tissue sarcoma lines HT-1080 and HS-18," Clinical Cancer Research, Vol. 6, Abstract 208, November 7-10, 2000		

Substitute for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
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/C.S./		Takahashi et al., "Sequence-dependent Enhancement of Cytotoxicity Produced by Ecteinascidin 743 (ET-743) with Doxorubicin or Paclitaxel in Soft Tissue Sarcoma Cells," Clinical Cancer Research, 7: 3251-3257 (October 2001)	
/C.S./		Takahashi et al., "Sequence-dependent Synergistic Cytotoxicity of Ecteinascidin-743 and Paclitaxel in Human Breast Cancer Cell Lines in Vitro and in Vivo," Cancer Research, 62: 6909-6915 (Dec. 1, 2002)	
/C.S./		Ten Hagen et al., "Pegylated Liposomal Tumor Necrosis Factor-Alpha Results in Reduced Toxicity and Synergistic Antitumor Activity after Systemic Administration in Combination with Liposomal Doxorubicin (Doxil) in soft tissue Sarcoma-Bearing Rats," Int. J. Cancer, vol. 97, pages 115-120, 2002	
/C.S./		Twelves, C.J. et al., "Phase I clinical and pharmacokinetic (PK) study of ecteinascidin-743 (ET-743) given as a one hour infusion every 21 days," 1998 ASCO Annual Meeting Proceedings, Abstract No. 889, 1998	
/C.S./		Twelves, C.J. et al., "Phase I and pharmacokinetic study of ecteinascidin-743 (ET-743) given as a one hour infusion every 21 days," ECCO, vol. 9, Abstract No. 1107, September 18, 1997	
/C.S./		Twelves et al., "A Phase I and Pharmacokinetic (PK) study of Et-743 evaluating a 3 hours (h) intravenous (iv) infusion (I) in patients (pts) with solid tumors," Clinical Cancer Research, Abstract #307, 5 (11, suppl. 3790S-3791S), November 16-19, 1999	
/C.S./		Twelves et al., "Phase I Trials with ET-743, a marine derived (MD) anticancer agent," Eur. J. Cancer, vol. 35, suppl. 4, page S283, Abstract No. 1135, Sept 15, 1999	
/C.S./		Valoti, G., et al., "Ecteinascidin-743 (ET-743), a marine natural compound, shows antitumor activity against human ovarian carcinoma xenografts," European Journal of Cancer (Novel Therapeutics and Pharmacology), vol. 34, Supp. 2, pageS39, Abstract PP179, 1998	
/C.S./		Valoti, G. "Ecteinascidin-743, a New Marine Natural Product with Potent Antitumor Activity on Human Ovarian Carcinoma Xenografts," Clin. Cancer Res., vol. 4, pages 1977-83, August 1998	
/C.S./		van Kesteren et al., "Pharmacokinetics and Pharmacodynamics of the Novel Marine-derived Anticancer Agent Ecteinascidin 743 in a Phase I Dose-finding Study," Clinical Cancer Research, vol. 6, pages 4725-2732, December 2000	
/C.S./		van Kesteren et al. "Clinical Pharmacology of the Novel Marine-derived Anticancer Agent Ecteinascidin 743 Administered as a 1- and 3-h Infusion in a Phase I Study," Anti-Cancer Drugs, Vol. 13, No.4, pgs. 381-393, April 2002	
/C.S./		van Kesteren et al. "Yondelis® (trabectedin, ET-743): The Development of an Anticancer Agent of Marine Origin" Anti-Cancer Drugs, Vol. 14, No.7, pgs. 487-502, August 2003	

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/C.S./		Villalona-Calero, M. et al., "A phase I and pharmacokinetic study of ET-743, a novel DNA minor groove binder of marine origin, administered as a 1-hour infusion daily x 5 days," Annals Oncology, Abstract 453, 1998	
/C.S./		Villalona-Calero, M. et al., "Final results of a Phase I and pharmacokinetic (PK) study of the marine minor groove binder ET-743 on a daily x 5 schedule," 1999 ASCO Annual Meeting Proceedings, Abstract No. 691, May 15-18, 1999	
/C.S./		Weiwei et al., "Potent antitumor activity of ET-743 against human soft tissue sarcoma cell lines," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 305, November 16-19, 1999	
/C.S./		Wiesenthal, "Is one 'sensitive' drug better than another?" downloaded from internet website << http://weisenthal.org/feedback.html >>, Feb. 4, 2002	
/C.S./		Wright et al., "Antitumor Tetrahydroisoquinoline Alkaloids from the Colonial Ascidian Ecteinascidia Turbinata", J. Org. Chem., vol. 55, pp. 4508-4512, 1990	
/C.S./		Zepek et al., "Preliminary results of phase II study of ecteinascidin (ET-743) with the 24 hour (H) continuous infusion (CI) q3week schedule in pretreated" Clinical Cancer Research, vol. 6, Supplement, Abstract 212, pages 4508s-4509s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
/C.S./		Zewail-Foote et al., "Ecteinascidin 743: A Minor Groove Alkylator that Bends DNA Toward the Major Groove," J. Med. Chem. 42, 2493-7, July 15, 1999	

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